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A RETROSPECTIVE ANALYSIS OF PLASMA SEX HORMONE LEVELS IN MALE AND FEMALE PATIENTS WITH ANDROGENETIC ALOPECIA.

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ABSTRACT

Introduction: Androgenic alopecia (AGA) is characterized by progressive scalp hair loss. It is responsible for hair loss in both men and women, often manifesting in the 3rd and 4th decades of life. AGA pathogenesis is linked to hormonal imbalance and genetic predisposition. In practice determination of serum levels of sex hormone, is prerequisite for AGA diagnosis. Here, we retrospectively examined the serum levels of five sex hormones in patients with androgenic alopecia, compared to levels in those without alopecia. **Materials and Methods:** A retrospective observational study was conducted at Zhongnan Hospital of Wuhan University from January 2022 to February 2023. Serum levels of five sex hormones were analyzed in androgenic alopecia patients and non-alopecia controls. **Results:** A total of 78 cases, and 94 controls were analyzed. 47 (60.2%) of the cases were males, and the mean (±SD) age were 31.84±5.42 vs 27.23±7.05 years for the cases and controls respectively. 55.1% of cases had family history of alopecia. In males, Testosterone, and Estrogen were all significantly higher in cases than controls, (all $p < 0.05$), while Follicle stimulating hormone, and Luteinizing hormone were lower in cases than controls (all $p < 0.05$). In females, Testosterone and Prolactin were significantly higher in cases than controls (all $p < 0.05$), while Follicle stimulating hormone, and estrogen were significantly lower in cases than controls (all $p < 0.05$). **Conclusions:** High levels of Testosterone were observed in the alopecia patients compared to non-alopecia individuals in both genders, and this could be linked to the alopecia.

KEYWORDS: Androgenic; Alopecia; Sex Hormones; Testosterone; Prolactin.

INTRODUCTION

Androgenic alopecia (AGA) is characterized by progressive miniaturization of the hair follicles resulting into gradual shrinkage of hair in the scalp, receding of the hairline and the characteristic "Horseshoe" shaped baldness often seen in men.[1] It is the most common cause of hair loss in both men and women, with an onset usually in the 3rd and 4th decades of life.[2,3] The estimated global prevalence of AGA is between 30% to 50%, while in China if affects 41.4% of men and women aged 18 to 29 years, and 11.8% of people older than 70 years.[3] Due to the constantly changing modern lifestyle and chemical use, including drinking and smoking, more young people are beginning to experience AGA than before, making it a significant challenge on the esteem and mental health of young men and women.[4]

The pathogenesis of AGA is multifactorial; tightly linked to the interactions between hormonal imbalance and genetic predisposition.[5] In men, it is specifically associated with androgen hyperactivity and genetic predisposition, while in females, its etiology is complex and still not well understood, although androgens and estrogen imbalance are implicated.[6] In individuals with androgenic alopecia, Testosterone is converted to Dihydrotestosterone (DHT) by an enzyme called 5 α-Reductase, and this new form of Testosterone starts to interfere with hair growth, in the process shortening the hair growth cycles, and consequently inducing hair loss.[7] A community based study conducted in Germany demonstrated that the hair follicles of people with alopecia have hyper-responsiveness to DHT, and so it is the hyper-responsiveness that induces alopecia, not necessarily increased levels of DHT,[5] however this is yet to be clarified in further studies.

In the clinical management of patients with alopecia, dermatologists often first determine the patient's sex hormone levels to ascertain whether any androgen imbalance exists that may induce baldness.[9] Main focus is often on the serum levels of Testosterone and its derivative DHT since these are the most closely associated with AGA.[10] In this study, we retrospectively examined the serum levels of the sex hormones; Testosterone, Follicle stimulating hormone, Luteinizing hormone, Estrogen, and Prolactin in a group of patients

with androgenic alopecia, and compared it with the levels in control individuals without alopecia. We also assessed other sociodemographic characteristics of the patients such as age, family history and lifestyle in order to determine which of them could be associated with androgenic alopecia in our setting.

MATERIALS AND METHODS

This was a retrospective observational study conducted at the Dermatology unit of Zhongnan Hospital of Wuhan University from January 2022 to February 2023. The study was approved by Zhongnan Hospital Research Ethics Committee and patient consent waived by the committee as the data were retrospectively collected. A total of 78 adult male and female patients aged 18 years and above, with androgenic alopecia, and 94 control group individuals without alopecia were recruited and analyzed. Patients were recruited based on clinical symptoms and the results of trichoscopic examination, diagnosis of androgenic hair loss by the dermatologists, and having no other skin diseases and illnesses that can cause hair loss. Information on the patients and control group on sociodemographic features, history of smoking or alcohol consumption, family history of hair loss, and results of serum levels of the sex hormones were extracted from the electronic medical database. Results of the sex hormones were interpreted according to the reference ranges established for Han Chinese people by Qin et al.[11]

Statistical analysis

Statistical data analysis was conducted in Statistical Package for Social Sciences (SPSS. Version 25.0). Normally distributed data were expressed as mean ± standard deviation, while categorical data were summarized as counts and percentages. Independent sample t test was performed to compare the mean difference of age and sex hormones between the cases and controls, while Pearson's Chi-square test or Fisher's exact test was used for categorical data. Statistical significance was set at $p < 0.05$.

RESULTS

General patient characteristics

A total of 78 patients with androgenic alopecia (cases), and 94 individuals without alopecia (controls) were recruited and analyzed. 47 (60.2%) of the cases were males, with 31 (39.8%) females. The Cases had a mean (±SD) age of 31.84±5.42 years, while the mean (±SD) age of the controls was 27.23±7.05 years. Majority of the cases (55.1%) had family history of alopecia, and some had history of smoking and alcohol intake. Detailed information on the patients is presented in **Table 1**.

Comparison of levels of sex hormones between alopecia Patients and Normal individuals

Next, we compared the serum levels of the sex hormones, (Estrogen, Prolactin, Testosterone, Follicle stimulating hormone and Luteinizing hormone) between the patients with alopecia, and control individuals without alopecia. Among the males, Testosterone, and Estrogen were all significantly higher in the cases than the controls, (all $p < 0.05$), while Follicle stimulating hormone, and Luteinizing hormone were lower in cases than in controls (all $p < 0.05$). Prolactin, though slightly higher in cases than in controls, was not statistically significant, ($p = 0.437$). Among the females, Testosterone and Prolactin were significantly higher in cases than in controls (all $p < 0.05$), while Follicle stimulating hormone, and estrogen were significantly lower in cases than in controls (all $p < 0.05$). Although Luteinizing hormone was slightly lower in cases than in controls, the difference was not statistically significant ($p = 0.051$). **Table 2.**

DISCUSSION

In this study, we examined the difference in the serum levels of sex hormones in patients with alopecia, versus individuals without alopecia for both men and women. In men, our results demonstrated that Testosterone, and Estrogen were significantly higher in patients with alopecia than in those without, while Follicle stimulating hormone and Luteinizing hormone were lower in alopecia patients than in those without. Prolactin on the other hand, though slightly higher in alopecia, was not significant.

The involvement of androgens in male pattern baldness, was first demonstrated in 1940,[12] and has since been established as a causative factor for hair loss in men. Hair growth in men is controlled by Testosterone (mainly produced form the testicular cells and some small amount in the adrenal cortex); meaning the higher it is, the more hair a male will grow,[13] However, when Testosterone is converted to Dihydrotestosterone (DHT) by an enzyme called 5 α- Reductase, this new form greatly interferes with hair growth, shortening the hair growth cycles, and consequently inducing hair loss.[14,15] In this study, the alopecia patients had significantly higher levels of testosterone than control groups which could have exposed them to higher rates of conversion of the Testosterone to DHT hence promoting hair loss. Recent population based studies have argued that it is not the high level of Testosterone than causes hair loss, but rather a sharply increased hair follicles sensitivity to DHT, which could be genetically determined, since a lot of men with increased levels of Testosterone do not develop alopecia.[8,6] In this study, we also noticed that some control individuals had higher levels of Testosterone than some alopecia patients, it is therefore likely that even our patients may have had higher sensitivity to DHT rather than the high Testosterone being the cause of the alopecia. Further studies are needed to resolve this.

Literature on the roles of Follicle stimulating hormone, and Luteinizing hormone in male hair loss are still scarce. However, estrogen and prolactin are known to influence androgen metabolism and so somehow contribute to male hair loss. Estrogen inhibits the enzymatic activity of aromatase; an enzyme responsible for converting

androgens into estradiol (E2),[17] while Prolactin is associated with inhibition of hair shaft elongation and the premature induction of the catagen phase.[18] It also plays a significant role in the proliferation and apoptosis of keratinocytes in the hair follicles.[18]

Generally, androgenic alopecia has the same mechanism in both men and women. In women just like in their male counterparts, dihydrotestosterone binds to the androgen receptors in susceptible hair follicles, and the hormone-receptor complex activates the genes responsible for the gradual transformation of large terminal follicles in to miniaturized follicles.[19] In this study, serum levels of Testosterone and prolactin were higher in the alopecia women while Follicle stimulating hormone, Luteinizing hormone and estrogen were all lower in alopecia women. This finding is consistent with results from Carmina et al.[20] who also demonstrated that female pattern hair loss was associated with altered levels of Testosterone and other sex hormones. Unlike men, the onset of female pattern hair loss is relatively early.[19] This was also observed in this study as the female alopecia patients had a lower mean age (31.88±8.25 years) compared to their male counterparts (32.5±3.8 years). The reduction in the serum level of estrogen seen among the alopecia women in this study is often seen in menopausal women. During menopause, the level of estrogen suddenly declines,[21] while androgens decline more gradually, creating an imbalance where androgen production; sustained by luteinizing hormone becomes more than estrogen, hence inducing various body changes including hair thinning and loss.[22] While Testosterone and its derivative DHT are well known inducers of hair loss in both men and women, the noticeable imbalance seen in the other sex hormones between alopecia and non-alopecia individuals, including, in this study may contribute more to hair loss than is currently known. Further studies are therefore required to clarify these findings.

Table 1: Patient characteristics.

Variables	Cases (n = 78)	Controls (n = 94)	p-value
Age, mean (SD)	31.84±5.42	27.23±7.05	0.013*
Gender, n (%)			0.042*
Male	47 (60.2)	52 (55.3)	
Female	31 (39.8)	42 (44.7)	
Family history, n (%)	43 (55.1)	2 (2.1)	0.038*
Smoking, n (%)	17 (21.8)	19 (20.2)	0.654
Alcohol, n (%)	9 (11.5)	14 (14.9)	0.532
Skin disease, n (%)	3 (3.8)	1 (1.1)	0.723

*Statistical significance. SD: Standard deviation

Table 2: Serum levels of sex hormones in alopecia patients and non-alopecia individuals.

	Males			Females		
Variables	Cases (n = 48)	Controls (n = 49)	p-value	Cases (n = 31)	Controls (n = 42)	p-value
TT(ng/ml)	4.92±1.53	3.91±1.36	0.024*	0.48±0.14	0.21±0.13	0.021*
FSH (mIU/ml)	4.10±1.95	4.97±1.45	0.047*	7.92±3.22	13.97±4.21	<0.001*
LH (mIU/ml)	5.27±2.23	5.96±2.49	0.033*	13.17±5.62	15.91±3.66	0.051
Estrogen (pg/ml)	27.82±9.36	23.85±8.94	0.048*	111.80±23.12	114.79±31.33	0.049
Prolactin (ng/ml)	15.93±6.62	14.9±5.41	0.437	25.99±5.34	18.79±4.11	0.011*
Age	32.5±3.8	23.4±1.9	<0.001*	31.88±8.25	30.48±7.51	0.215

TT: Testosterone. *Statistical significance. FSH: Follicle stimulating hormone. LH: Luteinizing hormone

CONCLUSION

In summary, androgenic alopecia in both men and women is induced by increased susceptibility of hair follicles to DHT, a derivative of the sex hormone, Testosterone. High levels of Testosterone were observed in the alopecia patients compared to non-alopecia individuals in both males and females, and could be linked to the alopecia. Although the other sex hormones were also dysregulated between the two groups of patients in both sexes, their contribution to hair loss is still not entirely clear and so further studies are needed to clarify.

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Author contribution
SN: Conceived the study, conducted data collection, data analysis and wrote the draft manuscript.
XJ: Reviewed the manuscript and supervised the study.

Conflict of interest
The authors declare no conflict of interest.

Ethical approval

Permission to conduct the study was obtained from the Zhongnan Hospital of Wuhan University Research Ethics Committee

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